

REMARKS

Entry of this Amendment is proper under 37 C.F.R. 1.116, because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration, and places the application in better form for an appeal should an appeal be necessary.

As noted in the Office Action Summary, claims 1, 5-7, 10-12 and 18-28 are pending. Claims 1, 10-12, 18 and 22-28 are amended herein. Basis for the amendments may be found throughout the specification and claims as-filed, especially at page 19, line 26 to page 20, line 4. Basis for the new claims may be found throughout the specification and claims as-filed, especially as indicated below:

Claim 32	Page 10, line 7
Claim 33	Page 10, line 8
Claim 34	Page 20, lines 29-32
Claim 35	Page 21, lines 36-37
Claim 36	Page 21, line 6
Claim 37	Page 21, lines 15-21
Claim 38	Page 21, lines 21-27
Claim 39	Page 22, lines 22-24
Claim 40	Page 22, lines 24-30
Claim 41	Page 22, lines 31-33
Claim 42	Page 23, lines 3-6
Claim 43	Page 23, lines 11-13

Claim 44	Page 23, line 37
Claim 45	Page 25, lines 7-26
Claim 46	Page 26, lines 13-17
Claim 47	Page 26, lines 20-21
Claim 48	Page 26, lines 32-34

Thus, no prohibited new matter is presented herein.

Claims 5-7, and 19-21 are canceled herein, the remaining pending claims are addressed below.

Applicants reserve the right to file at least one continuation or divisional application directed to any subject matter canceled by way of the present Amendment.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1, 5-7, 10-12 and 18-28 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which applicants regard as the invention. More specifically, the Examiner contends that the method as currently claimed is incomplete and omits several important steps, i.e. the recovery of virus from a producer cell line, the treatment of virus with benzonase and TWEEN®-80 to remove cellular debris, and recovery of the virus by some types of filtration process.

In the interest of expediting the prosecution of the instant application, claim 1 has been amended so as to recite the steps of (a) producing, (b) harvesting the virus preparation from the producer cells, and the optional steps of (c) breaking (i.e. lysis)

the producer cells, (d) clarifying the cell lysate and (f) purifying the viral particles, as requested by the Examiner. In view of these amendment, the rejection is obviated and Applicants respectfully request that it be withdrawn

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1, 5-7, 10-12 and 18-28 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly for lack of enablement. More specifically, the Examiner asserts that the disclosure fails to provide a sufficient number of method steps to perform and complete the claimed methodology and fails to provide a reasonable number of working examples.

In addressing the method steps, it is believed that the amendments discussed above in connection with 35 U.S.C. § 112, second paragraph, render this rejection moot. Applicants point out that the method of inactivating contaminating enveloped viruses in an adenoviral preparation can fit into any process of producing and purifying adenoviral particles from a producer cell line. For example, some processes include a lysis step and clarification is required to eliminate the cell debris whereas in others the viral preparation is harvested directly from the cell supernatant so as clarification is not required. Moreover, the adenovirus preparation once treated by TNBP can be purified by any technique in the art permitting to separate adenovirus particles from cellular contaminants, such as chromatography or centrifugation techniques. It should be noted that none of the methods known in the art for production and purification of therapeutic adenoviral particles for human use, addressed the question of inactivating enveloped viruses.

Turning to the Examiner's assertion that Applicants have failed to provide a reasonable number of working examples, Applicants draw the Examiner's attention to the fact that the instant claims are now directed to a method of preparing a viral preparation comprising an inactivation protocol involving TNBP at a concentration comprised between 0.1% and 0.6% and TWEEN®-80 at a concentration comprised between 0.5 and 2% where the TNBP and TWEEN®-80 are allowed to act at a temperature comprised between 4°C and 37°C, and at a pH of between 6.5 to 8.5. The solvent in the claimed method is clearly specified (TNBP) within a defined range of concentration (0.1-0.6%), the detergent is clearly specified (TWEEN®-80) within a defined range of concentration (0.5-2%), the reaction conditions are clearly specified (temperature between 4 and 37°C and pH between 6.5 and 8.5). Therefore, the question of utilizing any other solvents, detergents or reaction conditions is no longer an issue.

With respect to the Examiner's assertion that only the inactivating method involving TNBP at a concentration of 0.3% and TWEEN®-80 at a concentration of 1% at a pH of 8.5 is supported by the specification, Applicants submit that those conditions constitute the optimal conditions. However, concentrations of TNBP and TWEEN®-80 and the pH are flexible and can be adapted beyond the optimal values and within the ranges recited in the pending claims by one skilled in the art without undue experimentation.

In reply to the Examiner's assertion that only a temperature of 4°C is supported by the specification, Applicants submit that adenoviruses tolerate a large range of temperature up to 37°C without losing their activity. Moreover, Applicants direct the Examiner's attention to Example 1 which illustrates that the inactivation

protocol was successfully practiced by the inventors at a temperature of either 4°C or room temperature (about 25°C) (see the specification at page 32, line 20-23).

Therefore, the range of temperature recited in claim 1 is appropriate to successfully practice the claimed method.

In addition, concerning the presence of benzonase as mentioned on page 2 of the Office Action, Applicants would like to clarify that this enzyme is a nuclease and is not involved in the inactivation of enveloped virus. It is well known in the art that benzonase permits degradation of unencapsulated nucleic acids (e.g. cellular DNA and RNA) present in huge quantity in the viral preparation after cell lysis. Therefore, benzonase is not a required element of Applicant's claimed invention as set forth in claim 1.

In light of the above, Applicants request that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

FORMAL MATTERS

The Examiner objects to the use of the term "Tween" in the specification without the proper trademark symbol. Applicants have amended the specification and claims to properly identify the trademark symbol thereby rendering this objection moot.

Conclusion

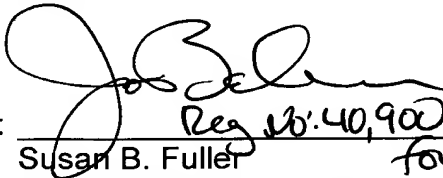
All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and as such, the present Application is in condition for allowance. If the Examiner believes for any reason that personal communication will expedite prosecution of this Application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: September 14, 2005

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